Integrative Actionable Tumor Investigations
Cancer is a genetic disease. Every human being is different and unique, so is his/her cancer. However, the conventional ‘standard of care’ approaches are based on population studies, which disregard the unique genetic landscape and complex metabolic dynamics of the tumor. As a result, the patients are at risk of failed therapies or aggressive relapse. It is, thus imperative that the genetic architecture of the tumor is studied comprehensively before deciding the treatment plan, which has to be personalised to the individual patient and his/her disease.

**Exacta® is a comprehensive, in-depth, integrative, cellular, and molecular tumor analysis, which parses millions of data points to present actionable vulnerabilities of the tumor for effective treatment strategies.**

Exacta® multi-analyte and multi-coordinate investigations that integrate genomic alterations in >400 genes and perturbation in expressions of 20,800 genes to unravel actionable mutations and pathways propelling cancer. Exacta® can identify the most efficacious drugs for every individual cancer and thus enables highly sophisticated treatment strategies beyond conventional perspective, even for difficult refractory cancers.
Exacta® is particularly recommended for cancer patients where...

- First-line therapy has failed
- Cancer has relapsed
- Cancer is high-grade/metastatic
- Newly diagnosed patients with difficult cancers
- Cancers with limited/no standard options
- The risk of therapy failure is high

### Exacta® methodology

**TARGETED GENES**
- SNVs, CNVs, Indels, Tumor Mutation Burden, Germline Mutations

**RNA**
- KEGG pathways (Disease, Actionable, Resistance), Gene Expression, Fusion/Rearrangement

**Pharmacogenetics**
- Genotyping for CYP450 metabolizing enzymes, drug transporters for drug toxicity and efficacy

**Chemosensitivity**
- In-vitro cell-based assay for testing cytotoxic drugs and drug combinations

**IHC*/ICC**
- Analysis of expression of various therapy relevant protein markers

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**SNVs**: Single Nucleotide Variations (Point Mutations)

**Indels**: Insertions and Deletions

**CNVs**: Copy Number Variations

**ICC**: Immunocytochemistry

**IHC***: Immunohistochemistry (if tissue sample is available)
Optimal Targeted Therapies:

Exacta®: A comprehensive molecular analysis that includes all relevant biomarkers, including mutations, deletions, gene rearrangement, gene amplification, and gene expressions, to identify tumor vulnerabilities for optimum targeted therapy selection. Exacta® also analyses the confounding impact of concurrent molecular indications for resistance and sensitivity, thus facilitating improved therapy selection compared to single gene test-based therapies.

Optimal Cytotoxic Therapies:

Exacta® not only evaluates response/resistance to cytotoxic drugs based on genetic analyses but also includes *in vitro* chemosensitivity testing on live tumor cells to ascertain the effect of cytotoxic drugs.

Optimal Immunotherapy:

Exacta® analyses clinical biomarkers such as PD-L1, Tumor Mutation Burden, and Micro Satellite Instability (MSI or germline MMR gene analysis) for selecting optimum immunotherapy agents, based on the sample type provided.

Drug Toxicity/Adverse Drug Reactions:

Exacta® aids selection of therapies with minimal side effects and best tolerance based on analysis of germline variants in drug metabolizing enzymes (DME) which are linked to drug toxicity and prediction of Adverse Drug Reactions (ADR).

Drug Repurposing:

In case of recurrent or high-grade cancers which have progressed despite prior therapy, Exacta® can explore additional therapeutic options via analysis of the molecular features of the tumors.

Therapy Recommendation:

Proprietary Exacta® analysis can provide the treating physician a curated list of individualised treatment strategies for on request and at an additional cost.
## Comprehensive Exacta®

### Parameters and Methods of Analysis: Exacta® (Tissue-Based)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Method</th>
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<td>Tumor DNA analysis (511)</td>
<td>Pharmacogenetics guidance</td>
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<tr>
<td>Gene rearrangements (RNA)</td>
<td>Microsatellite instability</td>
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<tr>
<td>Gene amplification/CNV</td>
<td>Tissue tumor mutational burden</td>
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<tr>
<td>KEGG pathways: Kyoto Encyclopedia of Genes and Genomes</td>
<td>PD-L1 IHC (Dako 22C3 and 28-8, Ventana SP142 in relevant cancer)</td>
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<tr>
<td>Cell-free DNA (52 genes)</td>
<td>Other therapy relevant IHC markers (ER, PR, AR, HER2)*</td>
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<tr>
<td>Gene expression (20,800 genes)</td>
<td>Circulating Tumor Cells (CTCs)</td>
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<tr>
<td>Cytotoxic therapy guidance (in vitro chemosensitivity on live tumor cells)</td>
<td>Therapy relevant ICC markers (mTOR, VEGFR1, VEGFR2, EGFR, VEGFA)</td>
</tr>
<tr>
<td>C-TAC-based in case of FFPE block</td>
<td></td>
</tr>
</tbody>
</table>

*Depending on the type of cancer*

- **CNV**: Copy Number Variation  
- **C-TACs**: Circulating Tumor-Associated Cells  
- **MMR**: Mismatch Repair  
- **KEGG**: Kyoto Encyclopedia of Genes and Genomes  
- **FFPE**: Formalin-fixed, Paraffin-embedded  
- **Exosomal**
### Parameters and Methods of Analysis: Exacta® (Blood-Based)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Analysis Method</th>
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<tr>
<td>Cell-free DNA (411 genes)</td>
<td>Pharmacogenetics guidance</td>
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<tr>
<td>Gene rearrangements (RNA)</td>
<td>MMR</td>
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<tr>
<td>Gene amplification/CNV</td>
<td>Blood tumor mutational burden</td>
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<tr>
<td>KEGG pathways: Kyoto Encyclopedia of Genes and Genomes</td>
<td>Circulating Tumor Cells (CTCs)</td>
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<tr>
<td>Gene expression (20,800 genes)#</td>
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- **MMR**: Mismatch Repair
- **KEGG**: Kyoto Encyclopedia of Genes and Genomes
- **FFPE**: Formalin-fixed, Paraffin-embedded
- **# Exosomal**
100s of millions of data points analyzed
(from peripheral blood and/or fresh tissue and/or FFPE block)

Blood-Based
- Cell-free DNA
- Exosomal Transcriptome
- Circulating Tumor Cells
- Chemosensitivity

Tissue-Based
- Tumor DNA analysis
- Cell-free DNA
- Transcriptome
- Circulating Tumor Cells
- Chemosensitivity

Driver Mutations; Gene Rearrangements; Insertions and Deletions
Tumor Cell Cycle Pathways; Identification of drugs with/without benefit

Database-based, multi-level iterative Colossus Algorithm to determine optimum (most favourable + least toxic) drugs and drug combinations

Clear, unambiguous, clinically actionable therapy relevant comprehensive information

Sample Requirement
- Peripheral blood as per our protocol
- Fresh tissue from biopsy / surgery (in our media) is preferred;
- Alternatively, FFPE tissue block